# 11th International Symposium on Trace Elements in Man and Animals

## Introduction[1]

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More than 265 delegates from 25 different countries attended the 11th International Symposium on Trace Elements in Man and Animals (TEMA) June 2–6, 2002, in Berkeley, CA. The theme for this symposium was "recent scientific advances and global implications for trace element nutriture in man and animals." To embrace this theme, the program featured an expanded scope from molecular and cellular functions of trace elements to human health effects of an imbalanced trace element intake. The format included plenary sessions, breakout sessions, poster presentations, workshops and opportunities for focused discussions during breaks and at the end of each day. The complete program and abstracts presented at the meeting can be viewed on the Internet at http://tema.ucdavis.edu/TEMA_abstracts.pdf.

TEMA, an organization that encourages the study of trace elements in animals and man, has been meeting every three years for about 35 years. The first TEMA symposium was held in Aberdeen, Scotland in 1969. Thereafter symposia were held in Madison, WI U.S.A. in 1973; Freising, Germany in 1977; Perth, Australia in 1981; Aberdeen, Scotland in 1984; Monterey, CA U.S.A. in 1987; Dubrovnik, Croatia in 1990; Dresden, Germany in 1993; Banff, Canada in 1996 and Evian, France in 1999. The 12th TEMA symposium will be held in Northern Ireland in 2005. The organization is governed by an international parent committee that is composed of the following individuals: Prof. Joseph R. Prohaska (chairman), University of Minnesota, Duluth, MN U.S.A.; Dr. John R. Arthur (secretary/treasurer), Rowett Research Institute, Aberdeen, Scotland; Prof. Roger Sunde, University of Missouri, Columbia, MO U.S.A.; Prof. Janet King, Children's Hospital Oakland Research Institute, Oakland, CA U.S.A.; Prof. Rosalind Gibson, University of Otago, New Zealand; Dr. Nick D. Costa, Murdoch University, Perth, Australia; Prof. Alain Favier, University of Grenoble, France; Dr. Peter W. F. Fischer, Health Canada, Ottawa, Canada and Prof. (Sean) J. J. Strain, University of Ulster, Coleraine, Northern Ireland.

The problem of trace element imbalances is truly a global issue, and evidence now shows trace element imbalances as a risk factor for a number of health problems. Correcting these imbalances involves using new knowledge of trace element function in novel public health problems. This issue was a major focus of the symposium; the keynote addresses in the opening session provided new information on the role of trace elements in maintaining the signaling function of nitric oxide, on effectively incorporating that knowledge into novel programs for correcting trace element deficiencies and on developing new approaches for estimating trace element requirements that are based on knowledge of whole-body homeostasis.

The first plenary session focused on emerging functional endpoints of trace element status. Each of the subsequent breakout sessions provided additional information about selected functional endpoints of trace element deficiency: immunity, oxidative stress, neurocognitive function and development. Iron, zinc, copper and selenium are required for normal immune function. When the supply of these nutrients is inadequate, numerous activities of cells in both the innate and acquired branches of the immune system are impaired. The extent of the impairment in the immune system can be sufficient to increase the risk of morbidity and mortality due to viral, microbial and parasitic infections; reversal of the trace element deficiency restores immunocompetence. Iron and zinc are required for normal neurocognitive function. Studies on human infants suggest that iron deficiency causes irreversible changes in the chemistry of neurotransmitters, organization and morphology of neuronal networks and neurobiology of myelination. Although many studies link zinc deficiency to children's cognitive and motor functioning, a clear consensus is lacking, which highlights the need for additional research into the timing of zinc deficiency and the co-occurrence with other micronutrient deficiencies. The trace elements copper, zinc and selenium work together to provide a cytosolic defense against reactive oxygen and nitrogen oxide species. Copper, zinc–superoxide dismutase catalyzes the dismutation of superoxide to oxygen and hydrogen peroxide. The latter and other

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hydroperoxides are subsequently reduced by the selenoenzyme glutathione peroxidase. The concerted effects of these trace elements in reducing oxidative stress show the importance of having a balanced intake of all trace elements. Trace element deficiencies also cause developmental defects due to rapid changes in cellular redox balance, tissue oxidative stress, inappropriate patterns of cell death, alterations in the migration of neural crest cells and changes in the expression of key patterning genes. In addition to well-recognized congenital malformations, mineral deficiencies during perinatal development can result in behavioral, immunological and biochemical abnormalities that persist into adulthood.

The second plenary session and the subsequent breakout session on the second day of the symposium focused on the global problem of trace element undernutrition. Possibly 50% of the world's population is zinc depleted. Randomized, controlled trials have demonstrated the profound impact of zinc supplementation on reducing diarrheal disorders, pneumonia and malaria during the past decade. Studies have also shown that marginal zinc intake may alter fetal and neonatal growth. Various strategies have been used to combat these deficiencies including supplementation, food fortification and modification of food preparation and processing methods. Biotechnology represents a new strategy to improve trace element nutrition. Genetic engineering can be used to introduce gene coding for trace element binding proteins, to overexpress storage proteins and/or to increase the expression of proteins that are responsible for trace element uptake into plants. This work requires a comprehensive understanding of trace element uptake and distribution in plants and the utilization of trace elements by animals.

The third day of the meeting focused on cellular metal metabolism. New information on the cellular functions of iron, selenium, zinc and copper were presented in the morning plenary session and the breakout sessions throughout the day. Several presentations focused on the iron regulatory proteins and how they modulate the mRNA-encoding proteins that are involved in the transport, storage and use of iron. Several new potential mRNA targets for iron regulatory proteins recently identified, divalent metal transporter 1 and ferroportin, are critical regulators of iron absorption in the gut and iron cycling between various tissues of the body. Selenoprotein P, one of 10 additional selenoproteins recently identified, is an extracellular protein that contains most of the selenium in plasma. It appears to protect against oxidative injury and to transport selenium from the liver to peripheral tissues. Measures of selenoprotein P should be incorporated into studies of selenium status. Recent studies of the cellular function of zinc have focused on the role of zinc transporters. Zinc transporters help regulate the cellular supply of this micronutrient to maintain normal function. Cellular zinc depletion readily alters the expression of zinc transporters. Nearly a dozen different zinc transporters have been identified, which demonstrates the importance of maintaining a normal cellular zinc supply. Genetic defects in copper metabolism provide new information on the important role of this element in sustaining cellular iron homeostasis and function. In addition to concerns about the cellular and functional consequences of insufficient amounts of trace elements, excessive accumulation also needs to be considered. Two speakers focused on the toxic effects of excessive amounts of arsenic and mercury in the environment.

Workshops were scheduled on the morning of the last day of the meeting to provide the attendees with detailed information on new technologies and methods for studying trace elements. One workshop focused on the challenges of measuring zinc status. Another provided guidance on how to design and implement field-based trace element studies, and a third workshop reviewed emerging analytical methods that are available for quantitating trace elements.

In the closing session, two speakers summarized some of the new knowledge presented during the symposium. One presentation focused on the importance of integrating new findings about cellular trace element metabolism to the physiology and function of the whole organism and used copper as an example. The final speaker reviewed the impressive strides in understanding trace element metabolism, but many gaps still exist, i.e., how to precisely recognize trace element deficiencies, the basis for variation in trace element needs and the roles of genetics and dietary factors in determining trace element phenotype. Future studies need to integrate the genome with the metabolome so that the entire system and its strategy are understood, not just the component parts and their individual controls. This will be our challenge as we plan for the 12th International TEMA Symposium in Northern Ireland in 2005.